heparin containing blood. Each cannula was removed after the 24.00 hour sample was drawn or earlier or if blocked.

At the end of the study, the samples were transferred to the bio-analytical facility in a box containing sufficient dry ice to maintain the integrity of the samples. These samples were stored at a temperature of −70° C.±20° C. in the bio-analytical facility until analysis.

Progesterone (Corrected and Uncorrected) and Estradiol (unconjugated) and estrone (total) in plasma samples is assayed using a validated LC-MS/MS method.

The pharmacokinetic parameters Cmax, AUC0-t & AUC0-∞ were calculated on data obtained from 24 subjects for the test product and reference product. In general, bioavailability of progesterone and estradiol were similar but bioequivalence was not established.

Corrected pharmacokinetic profile summaries are presented in Table 9, below, for progesterone.

TABLE 9

Summary of Primary Pharmacokinetic Profile of Test Product (T) versus Reference Product (R) for Progesterone (Corrected)

	Geometric Mean*		Arithmetic Mean ± Standard Deviation	
Pharmacokinetic Parameter	Test Product (T)	Reference Product (R)	Test Product (T)	Reference Product (R)
C_{max}	47.0	43.0	81.0 ± 82.8	117.7 ± 173.7
AUC_{0-t}	107.6	97.8	163.9 ± 136.5	191.1 ± 241.7
$AUC_{0-\infty}$	110.7	110.0	173.5 ± 143.0	207.1 ± 250.3

*Estimate of Least Square Mean used to calculate Geometric Mean

Study **351**—Progesterone and Estradiol Combination Study under Fasting Conditions.

Fasted studies using the above protocol and test and reference products were also conducted. However, rather than the high-fat meal prior to administration of the test and reference drug, each subject fasted for a period of at least twelve (12) hours prior to dose administration.

The pharmacokinetic parameters Cmax, AUC0-t & AUC0-∞ were calculated on data obtained from 23 subjects under fasting conditions for the test product and reference product. In general, bioavailability of progesterone and estradiol were similar but bioequivalence was not established.

Corrected pharmacokinetic profile summaries are presented in Table 10, below for progesterone.

TABLE 10

Summary of Primary Pharmacokinetic Profile of Test Product (T) versus Reference Product (R) for Progesterone (Corrected)

	Geometric Mean*		Arithmetic Mean ± Standard Deviation	
Pharmacokinetic Parameter	Test Product (T)	Reference Product (R)	Test Product (T)	Reference Product (R)
C_{max}	2.3	3.0	2.9 ± 2.3	3.9 ± 3.4
AUC_{0-t}	8.4	10.9	11.2 ± 8.7	14.5 ± 11.0
$AUC_{0-\infty}$	12.9	17.2	15.1 ± 9.0	19.6 ± 10.2

*Estimate of Least Square Mean used to calculate Geometric Mean

The data indicate good (i.e., low) inter-patient and intra-patient variability relative to PROMETRIUM.

Example 14

Dissolution

Dissolution studies were performed using a formulation of this invention comparing the dissolution of progesterone to the dissolution of PROMETRIUM and comparing the dissolution of estradiol to the dissolution of Estrace. In one study, a formulation of the invention in capsules comprising 200 mg of progesterone and 2 mg estradiol was used. In a second study, a formulation of the invention in capsules comprising 50 mg of progesterone and 2 mg estradiol was used. The two formulations comprised:

The dissolution study was performed using a USP dissolution apparatus (reciprocating cylinder) ("USP Apparatus 3"). The apparatus was set to 30 dips per minute. 250 mL of a solution of 0.1N HCl with 3% sodium lauryl sulfate was used at 37 C.

In both studies, progesterone was dissolved faster, and with smaller standard deviations, from the capsules of the invention than from PROMETRIUM. Dissolution of estradiol was comparable but marginally slower from the capsules of the invention than from Estrace. For illustrative purposes, a graph showing progestrone dissolution from the 200 mg progesterone capsule of the invention and from PROMETRIUM is attached as FIG. **6**.

Both capsules of the invention were stable on storage in white HDPE bottles. Positive stability data were obtained with the 200 mg progesterone formulation over 6 months (>6 months data unavailable) and with the 50 mg progesterone formulation over 3 months (>3 months data unavailable).

It will be apparent to those skilled in the art that various modifications and variations can be made in the present disclosure without departing from the spirit or scope of the disclosure. Thus, it is intended that the present disclosure cover the modifications and variations of this disclosure provided they come within the scope of the appended claims and their equivalents.

Likewise, numerous characteristics and advantages have been set forth in the preceding description, including various alternatives together with details of the structure and function of the devices and/or methods. The disclosure is intended as illustrative only and as such is not intended to be exhaustive. It will be evident to those skilled in the art that various modifications may be made, especially in matters of structure, materials, elements, components, shape, size and arrangement of parts including combinations within the principles of the disclosure, to the full extent indicated by the broad, general meaning of the terms in which the appended claims are expressed. To the extent that these various modifications do not depart from the spirit and scope of the appended claims, they are intended to be encompassed therein.

What is claimed is:

1. A pharmaceutical composition comprising:

progesterone;

a medium chain oil; and a non-ionic surfactant;

wherein the progesterone is present from about 20 to about 50 weight percent of the composition.

2. The pharmaceutical composition of claim **1**, wherein the progesterone is ultra-micronized and has an X50 less than or equal to 15 microns.

3. The pharmaceutical composition of claim **2**, wherein the ultra-micronized progesterone has an X90 of less than about 25 microns.